CLAIMS

What is claimed is:

1. A bioreactor comprising:
   i. a first substrate having a first surface, an opposite second surface and edges;
   ii. a second substrate having a first surface and an opposite second surface, defining a cavity with a bottom surface, wherein the bottom surface is located therebetween the first surface and the second surface, and wherein the first surface of the first substrate is received by the second surface of the second substrate to cover the cavity so as to form a channel for receiving cells and a liquid medium;
   iii. a recess formed in the second substrate with a bottom surface and in fluid communication with the channel; and
   iv. a barrier positioned for covering the recess so as to form an outer chamber, wherein the barrier has a porosity to allow the channel and the outer chamber in fluid communication and control the move of at least one predetermined type of cells between the channel and the outer chamber.

2. The bioreactor of claim 1, wherein the second substrate further defines a first opening and an opposite, second opening adapted for allowing a flow of liquid to be introduced into the channel through the first opening and away from the channel through the second opening substantially along a first direction.

3. The bioreactor of claim 2, further comprising a biocompatible coating layer applied to the interior surfaces of the second substrate around the channel.

4. The bioreactor of claim 3, wherein the biocompatible coating layer comprises a material that may inhibit cell adhesion to the biocompatible coating layer, enhance cell adhesion to the biocompatible coating layer, promote organization and growth of cells, or function as a fluorescent marker or indicator of the state of cells.

5. The bioreactor of claim 3, wherein the channel is sized to allow the growth of a layer of cells on the biocompatible coating layer and the flow of liquid in the channel.

6. The bioreactor of claim 5, wherein the flow of liquid is controlled so as to provide a known shear force to the layer of cells.

7. The bioreactor of claim 5, wherein the flow of liquid is controlled so as to provide an environment that simulates a vascular space in the channel.

8. The bioreactor of claim 7, wherein the cells comprise endothelial cells.

9. The bioreactor of claim 8, wherein the layer of cells substantially forms an endothelial cells lined capillary in the channel.

10. The bioreactor of claim 9, wherein the channel is sized such that when at least one cell that is not one of the endothelial cells is introduced into the channel, it can undergo intravasation in the endothelial cells lined capillary.

11. The bioreactor of claim 9, wherein the at least one cell that is not one of the endothelial cells is a tumor cell.

12. The bioreactor of claim 9, wherein the second substrate further defines at least one injection port in fluid communication with the channel to allow a stream of substance to be introduced into the channel through the injection port substantially along a second direction.

13. The bioreactor of claim 12, wherein the second direction is substantially perpendicular to the first direction.

14. The bioreactor of claim 12, wherein the stream of substance is controlled so as to provide a gradient to the channel.

15. The bioreactor of claim 14, wherein the stream of substance comprises chemokine.

16. The bioreactor of claim 14, wherein the stream of substance comprises a substance affecting the growth of cells.

17. The bioreactor of claim 1, wherein the barrier comprises a plurality of posts spaced with a gap from each other.

18. The bioreactor of claim 1, wherein the outer chamber is sized to allow the growth of a host of cells.

19. The bioreactor of claim 18, wherein the host of cells comprises at least a first type of cells and a second type of cells that is different from the first type of cells.

20. The bioreactor of claim 19, wherein the first type of cells comprises normal cells.

21. The bioreactor of claim 20, wherein the second type of cells comprises tumor cells.

22. The bioreactor of claim 18, further comprising a port formed in the second substrate and a connection channel formed in the second substrate such that the connection channel is in fluid communication with the outer chamber and the port.

23. The bioreactor of claim 18, further comprises a plurality of electrodes adapted for electrochemical measurements of the host of cells.

24. The bioreactor of claim 18, further comprises a plurality of controlling ports and a plurality of connection channels, wherein each of the connection channels is in fluid communication with a corresponding controlling port and the outer chamber.

25. The bioreactor of claim 1, wherein the second substrate is fabricated from glass, Mylar, PDMS, silicon, a polymer, a semiconductor, or any combination of them.

26. The bioreactor of claim 1, wherein the first substrate is at least partially optically transparent.

27. The bioreactor of claim 26, wherein the dynamic activities of cells in the channel are detectable through optical detecting means.

28. A bioreactor comprising:
    i. a first substrate having a first surface and an opposite second surface, defining a chamber therebetween for receiving cells and a liquid medium;
    ii. an inlet port formed in the first substrate;
    iii. a first connection channel formed in the first substrate, wherein the first connection channel is in fluid communication with the inlet port and the chamber for allowing a stream of substance to be delivered to the chamber;
    iv. an outlet port formed in the first substrate;
    v. a second connection channel formed in the first substrate, wherein the second connection channel is in fluid communication with the outlet port and the chamber for allowing a stream of substance to be removed from the chamber; and
    vi. confining means positioned in a region in the chamber proximate to the first connection channel to confine the cells.

29. The bioreactor of claim 28, wherein the confining means comprises a plurality of traps, wherein each of the plurality of traps is capable of receiving at least one cell.

30. The bioreactor of claim 29, wherein each of the plurality of traps comprises a structure defining a recess so as to receive and confine at least one cell therein.

31. The bioreactor of claim 30, wherein the structure is partially formed with a filter to allow the recess to be in fluid communication with the chamber.

32. The bioreactor of claim 29, wherein the plurality of traps forms an array.

33. The bioreactor of claim 28, wherein the first substrate further defines a first alternate port and a third connection channel in fluid communication with the first alternate port and the first connection channel for allowing additional substance to be introduced into the chamber.

34. The bioreactor of claim 28, wherein the first substrate further defines a second alternate port, a third connection channel, and a second chamber, wherein the third connection channel is in fluid communication with second

alternate port and the second chamber, and the second chamber is in fluid communication with the first connection channel.

35. The bioreactor of claim 34, wherein the second chamber is formed with an oxygen permeable structure to provide oxygen to the cells.

36. The bioreactor of claim 28, wherein the first substrate is fabricated from glass, Mylar, PDMS, silicon, a polymer, a semiconductor, or any combination of them.

37. The bioreactor of claim 28, further comprising a second substrate having a first surface and an opposite, second surface, and means adapted for electrochemical measurements of the cells in the chamber, wherein the means for electrochemical measurements is positioned with the second substrate such that when the first surface of the second substrate is received by the second surface of the first substrate, the means for electrochemical measurements is at a corresponding measurement position.

38. The bioreactor of claim 37, wherein the means for electrochemical measurements comprises:

i. at least one electrode monitoring entry of the cells into the chamber;
ii. at least one electrode monitoring leaving of the cells from the chamber; and
iii. a plurality of electrodes detecting chemical species in the chamber.

39. The bioreactor of claim 28, further comprising a third substrate having a first surface and an opposite, second surface, and means adapted for optical measurements, wherein the means for optical measurements is positioned with the third substrate such that when the first surface of the third substrate is received by the second surface of the first substrate, the means for optical measurements is at a corresponding measurement position.

40. The bioreactor of claim 39, wherein the means for optical measurements comprises a plurality of optical sensors strategically positioned for detecting chemical and biological species within the chamber and the physiological state of the cells within the chamber.

41. The bioreactor of claim 39, wherein the third substrate is at least partially transparent.

42. A bioreactor comprising:

i. a first substrate having a first surface and an opposite second surface, defining a chamber therebetween for receiving cells and a liquid medium;

ii. an inlet port formed in the first substrate;

iii. a first connection channel formed in the first substrate, wherein the first connection channel is in fluid communication with the inlet port and the chamber for allowing a stream of substance to be delivered to the chamber;

iv. an outlet port formed in the first substrate;

v. a second connection channel formed in the first substrate, wherein the second connection channel is in fluid communication with the outlet port and the chamber for allowing a stream of substance to be removed from the chamber; and

vi. confining means positioned in the chamber to form a confinement region to confine the cells therein.

43. The bioreactor of claim 42, wherein the confining means comprises a first filter and a second filter, wherein the first filter is positioned proximate to the first connection channel and the second filter is positioned proximate to the second connection channel, and the first filter and the second filter are substantially parallel to each other.

44. The bioreactor of claim 43, wherein each of the first filter and the second filter comprises a plurality of posts spaced apart from each other not to allow cells to pass through it.

45. The bioreactor of claim 42, wherein the first substrate further defines a first alternate port and a third connection channel in fluid communication with the first alternate port and the confined region of the chamber for allowing seed cells to perfuse only outside the confined region in the chamber.

46. The bioreactor of claim 42, wherein the first substrate is fabricated from glass, Mylar, PDMS, silicon, a polymer, a semiconductor, or any combination of them.

47. The bioreactor of claim 42, further comprising a second substrate having a first surface and an opposite, second surface, wherein the second substrate is sized such that when the first surface of the second substrate is received by the second surface of the first substrate, the chamber is covered.

48. The bioreactor of claim 47, further comprising at least one supporting member positioned outside the confined region of the chamber for supporting the second substrate.

49. The bioreactor of claim 47, further comprising at least one supporting member positioned inside the confined region of the chamber for supporting the second substrate.

50. A bioreactor comprising:

i. a first substrate having a first surface and an opposite second surface, defining a first chamber therebetween for receiving a first type of cells and a liquid medium;

ii. at least one second chamber formed in the first substrate for receiving a second type of cells and a liquid medium;

iii. at least one connection channel formed in the first substrate, wherein at least one connection channel is in fluid communication with a corresponding second chamber and the first chamber for allowing the first type of cells and the second type of the cells to interact with each other.

51. The bioreactor of claim 50, wherein the first type of cells comprises protozoa.

52. The bioreactor of claim 51, wherein the second type of cells comprises bacteria.

53. The bioreactor of claim 52, wherein the connection channel is formed to allow protozoa to travel therein.

54. The bioreactor of claim 53, further comprising a sizing limiting post to limit the mobility of protozoa.

55. The bioreactor of claim 53, wherein the connection channel is formed with a cross-sectional dimension variable along the length of the connection channel to limit the mobility of protozoa.

56. The bioreactor of claim 53, further comprising a barrier positioned in the connection channel for separation of bacteria and protozoa.

57. The bioreactor of claim 50, wherein the first substrate is fabricated from glass, Mylar, PDMS, silicon, a polymer, a semiconductor, or any combination of them.